REMARKS

As an initial matter, Applicants respectfully request an interview with the Examiner prior to the mailing of an Advisory Action based on this response.

Claims 1-4, 11, and 12 are pending. Claims 5-10 and 13-77 have been cancelled. Claims 1, 4, 11, and 12 are currently amended. Support for the amendments to the claims can be found in the specification and claims as originally filed. In particular, support for the amendments can be found on page 5, lines 9-11, page 55 (Table 1), and page 57, lines 27-32. Accordingly, no new matter has been added.

Priority

The Examiner asserts that the effective filing date of the claims is April 25, 2003 – the filing date of PCT Application No. PCT/US03/12729 - and not April 26, 2002 – the filing date of Provisional Application No. 60/375,719 (the '719 application). The Examiner asserts that claims 1-4, 11, and 12 do not properly claim benefit to the earlier filing date under § 119 or § 120 because the claims stand rejected under 35 U.S.C. § 112. For the reasons set forth in the section of these remarks addressing the § 112 rejections, Applicants submit that the claims are neither indefinite nor lack enablement and, therefore, the claims are entitled to the benefit of the filing date of the '719 application.

In addition, the Examiner alleges that claims 1-4, 11, and 12 do not properly benefit under § 119 or § 120 to the '719 application's filing date because the '719 application does not provide support for the claimed process of "qualifying prostate cancer status in a subject." Applicants respectfully disagree.

The '719 application provides support for qualifying prostate cancer status in a subject. For example, the '719 application provides for "detecting at least one or more protein biomarkers in a subject sample, and; correlating the detection of one or more protein biomarkers with a diagnosis of cancer. . . ." Additionally, the '719 application defines "diseases of the prostate" or "prostate disease" as "any disease or condition of the prostate including, but not limited to, benign prostatic hyperplasia (BPH), prostatitis, prostatic intraepithelial neoplasia

(PIN) and cancer." '719 application, page 18, lines 17-20. Furthermore, the '719 application provides that "A major advantage of identification of these markers is their high specificity and ability to differentiate between different prostate disease states." '719 application, page 18, lines 6-7. Taken together a person of skill in the art would understand that the '719 application provides support for the instant claims directed to using specific biomarkers for qualifying prostate cancer status in a subject wherein qualifying prostate cancer status is determining the type of disease.

Claim Objections

The Examiner objects to claims 1-4, 11, and 12 for allegedly being directed to the subject matter of non-elected inventions. Applicants respectfully traverse the objection. Claim 1 has been amended. Amended claim 1 is directed to:

> A method of qualifying the prostate cancer status in a subject comprising: (a) measuring the amount of Marker I having a molecular weight of about 7.808 kD as measured by mass spectrometry in a biological sample from the subject, and (b) comparing the measured amount of Marker I to that of a control, wherein a decrease in the amount of Marker I as compared to a control is indicative that the subject has prostate cancer.

In a Response to Restriction Requirement dated April 27, 2007, Applicants elected the claims of Group III and made a species election of Marker I. The elected invention is drawn to a method of qualifying prostate cancer status in a subject, said method comprising measuring at least one biomarker in a sample from the subject, wherein said prostate cancer status is the type of disease. Applicants submit that the amended claims are drawn to the elected invention and species. On page 33, lines 28-30 the specification states, "The biomarkers of the invention are highly specific in detecting and differentiating between diseases of the prostate such as, for example, prostate cancer at any stage, BPH, and the like." A claim directed to the determination of whether a subject has prostate cancer is a claim directed to a determination of the type of disease because prostate cancer is one of the types of diseases provided for by the specification.

The Examiner objected to claim 1 for including a typographical error. This objection is overcome by the present amendment.

Rejection of Claims 1-4, 11 and 12 Under 35 USC 112, Second Paragraph

The Examiner rejected claims 1-4, 11, and 12 under 35 USC 112, second paragraph as allegedly indefinite. The Examiner asserts that the claims are directed to a method for qualifying prostate cancer status wherein prostate cancer status is the type of disease but that the claim merely recites a process for measuring the amount of Marker I. The Examiner alleges that the claim does not provide how the measurement is correlated with type of the disease. Applicants respectfully traverse the rejection.

Applicants have amended claim 1. As amended, claim 1 recites two process steps, namely a measuring step and a comparing step.

> A method of qualifying the prostate cancer status in a subject comprising: (a) measuring the amount of Marker I having a molecular weight of about 7.808 kD as measured by mass spectrometry in a biological sample from the subject, and (b) comparing the measured amount of Marker I to that of a control, wherein a decrease in the amount of Marker I as compared to a control is indicative that the subject has prostate cancer.

Applicants submit that the amended claims are not indefinite because they now fully recite how a measurement is correlated with a type of disease; the measured level of Marker I is compared to a control wherein a decrease in the amount of Marker I is indicative of a type of disease (prostate cancer).

Rejection of Claim 4 Under 35 USC 112, Second Paragraph

The Examiner alleges that claim 4 is indefinite because it is directed to "measuring the marker after subject treatment" but that according to claim 3 managing subject treatment includes "taking no further action." The Examiner asserts that it cannot be known or determined when the marker is necessarily measured afterward. Applicants respectfully disagree. As an initial matter, claim 4 depends from claim 2 not claim 3, and claim 2 does not recite the limitation "taking no further action." Based solely on this, Applicants submit that the rejection is improper. But even assuming *arguendo* that claim 4 must be read in light of the limitations of claim 3, claim 4 would not be indefinite. A person of skill in the art would understand that if the

subject management was "take no further action" then claim 4 would be performed if Marker I was measured at any time after the decision to "take no further action" was made. Applicants submit that the claim 4 is definite and respectfully request that the Examiner withdraw the rejection.

Rejection of Claims 1-4, 11 and 12 Under 35 USC 112, First Paragraph

The Examiner has rejected claims 1-4, 11, and 12 under 35 USC 112, first paragraph as not being enabled. In particular, the Examiner asserts that the specification teaches that Marker I is down-regulated in serum from men with prostate cancer compared to serum from men without prostate cancer, but the specification does not teach an association between the marker and the type of disease.

Applicants respectfully disagree. As defined in the specification, a determination that a subject has prostate cancer is a determination of the type of disease of the prostate. The specification teaches that prostate cancer is a type of disease of the prostate. For example, on page 18, lines 30-33, the specification defines "diseases of the prostate" as:

> As used herein, "diseases of the prostate" or "prostate disease," or "condition of the prostate," as used herein, refer to any disease or condition of the prostate including, but not limited to, benign prostatic hyperplasia (BPH), prostatitis, prostatic intraepithelial neoplasia (PIN) and cancer.

Additionally, the specification teaches that the biomarkers can be used to detect diseases of the prostate, including prostate cancer. For example, the specification provides on page 30, lines 28-30 that :

> The biomarkers of the invention are highly specific in detecting and differentiating between diseases of the prostate such as, for example, prostate cancer at any stage, BPH, and the like.

Clearly, the specification teaches that prostate cancer is a type of disease of the prostate and that a marker that is down-regulated in prostate cancer is one that is associated with a type of disease. Applicants submit that the amended claims are fully enabled because the specification teaches that Marker I is down-regulated in the serum of men with prostate cancer compared to the serum of un-afflicted men, and prostate cancer is a type of disease of the prostate.

Based on the June 8th Office Action, it seems that the Examiner is requiring the specification to be enabling for a single biomarker to distinguish between each and every type of disease of the prostate. However, the instant claims do not recite this as a limitation and the specification does not define a determination of a type of disease so narrowly.

Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

Rejection of Claims 1-4 Under 35 USC 102(b)

The Examiner has rejected claims 1-4 under 35 USC 102(b) as being anticipated by Cazares et al. (Clin. Cancer Res., 2002 Aug; vol. 8(8); pages 2541-2552). Applicants respectfully traverse this rejection.

The Examiner alleges that Cazares et al. teach biomarkers that are about 7.808 kDa. Specifically, the Examiner indicates that Cazares et al. teach biomarkers that have molecular weights of about 6.913, 7.368, and 8.238 kDa in Figure 1. Applicants respectfully disagree.

In a prior response, Applicants noted that the term "about" when referring to the mass of the biomarkers, is defined to include the variances in mass accuracy and in the operation of the instrument. The definition at paragraph [0017] defines the variances to be within 0.15% of the actual mass value. Accordingly, based on the teachings in the specification, a biomarker having a molecular weight of "about" 7.808 kDa will have a molecular weight that ranges from 7.796 kDa to 7.820 kDa. Clearly, biomarkers taught by Cazares et al. having masses of 6.913, 7.368, and 8.238 kDa are not within the range that is "about" 7.808 kDa.

The Examiner rejected Applicants' use of the definition of "about" on the grounds that the definition only refers to a molecular weight determined by mass spectroscopy and that claim 1 does not require that molecular weight be determined by mass spectrometry.

Without agreeing with the Examiner and solely to expedite prosecution, Applicants have amended claim 1. As amended, claim 1 is directed to Marker I having a molecular weight of about 7.808 kD as measured by mass spectrometry. Applicants submit that Marker I is a specific marker that was identified and defined by mass spectrometry, this is clearly illustrated in

Figure 1D. As the Examiner admits, the specification clearly defines the meaning of "about" as it relates to the measurement of molecular mass by mass spectrometry. Additional support is found on page 5, lines 9 to 11 of the specification which provides that "Molecular weights as measured by mass spectrometry are specified for each marker as follows: Marker I: having a molecular weight of about 7.808 kD." Applicants submit that Marker I is a specific marker that is clearly defined in the specification as having a mass value of about 7.808 kDa as determined by mass spectrometry (i.e., from 7.795 kDa to 7.820 kDa). Cazares et al. do not teach a marker of this size range and, therefore, do not anticipate claim 1.

Applicants submit that Marker I has a molecular weight of "about" 7.808 kDa as measured by mass spectrometry and that the specification teaches that "about" is considered to be within +/- 0.15 percent; therefore, the specification fully supports a claim directed to Marker I having a molecular weight from 7.795 kDa to 7.820 kDa. Cazares et al. do not teach a marker of this size range and, therefore, do not anticipate the claim 78.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

CONCLUSION

For at least the foregoing reasons, each of the presently pending claims in this application is believed to be in condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. Should any of the claims not be found to be in condition for allowance, the Examiner is requested to call Applicants' undersigned representative to discuss the application. Applicants thanks the Examiner in advance for this courtesy.

A Petition for a Two-Month Extension of Time, a Request for Continued Examination and the required fees accompany this response. Applicants believe that no other fees are due, however, the Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105. Refund of any overpayments is respectfully requested.

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Respectfully submitted,
Electronic signature: /Andrew W. Shyjan/
Andrew W. Shyjan
Registration No.: 61,294
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(617) 517-5595
Attorneys/Agents For Applicant